IMPLICATIONS OF CORONARY ARTERIOGRAPHY

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1974

YALE

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A thesis submitted in partial fulfillment

of the requirements for the degree of

DOCTOR of MEDICINE

YALE UNIVERSITY SCHOOL OF MEDICINE

MARCH, 1974

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AB, MAGNA CUM LAUDE, HARVARD COLLEGE, 1970

ACKNOWLEDGEMENT

I am deeply grateful to Dr. Steven Wolfson for his patient guidance in the preparation of this thesis. It has been a distinct pleasure to work with him.

Introduction

The history of cardiac catheterization in humans began in 1929 when Dr. Werner Forssmann passed a catheter through a vein in his own left arm to his right atrium. He then walked across the Auguste Viktoria Hospital and up a flight of stairs to the X-ray department where he was flouroscoped with the aid of a nurse holding a mirror and had chest X-rays taken to prove what he had done (Forssmann, 1929, translated by Mueller and Buekler). The history of complications of cardiac catheterization began that same day, when he fainted from blood loss after the X-rays were taken. Right heart catheterization gained acceptance in the 1940's, and left heart catheterization in the 1950's (Cournand, 1941; Braunwald, 1968a). Selective catheterization of the coronary arteries for cineangiography was developed in the late 1950's (Sones, 1962). The most common early complication was ventricular fibrillation, which was at first treated by open-chest cardiac massage, with a high mortality. Closed-chest massage and external defibrillation were substituted, and the mortality traceable directly to this arrhythmia dropped nearly to zero.

In 1968, the report of the Cooperative Study on Cardiac Catheterization, sponsored by the Scientific Council of the American Heart Association was issued. Of 3,312 coronary angiograms performed on adults, three

deaths resulted. Three other deaths were reported in patients who were catheterized for reasons other than suspected coronary artery disease and on whom no coronary angiography was attempted. Of these six deaths, one was related to dissection of the left main coronary artery, one to aortic perforation and hypovolemia, one to a cerebral embolus displaced from an aortic aneurysm, and one to subendocardial infarcts which may have been caused by anemia following hemorrhage from the femoral puncture site. Thus, technical errors were difinitely implicated in two deaths and may have contributed to two others (Braunwald, 1968b; Ross, 1968). Three other patients survived myocardial infarcts sustained during coronary angiography. One was due to a dissection of the right coronary artery, one to an embolus dislodged from a Starr-Edwards aortic valve, and one had no obvious cause. Thus, the emphasis of the report was on technical factors leading to complications in adult catheterization. This is in contrast to the case in pediatric catheterization, where complications seemed related to the critically ill status of these patients.

Some questions of technique have remained controversial. One report of four cases of fatal thromboembolism suggested that catheter stiffness, material, and coating may influence the rate of thromboembolic phenomena (Giddings, 1972). There is also disagreement as to the relative safety of the brachial arteriotomy

and percutaneous femoral arterial approaches. In the former, a flexible catheter is manipulated into the coronary ostia. The latter utilizes preformed catheters for the left and right coronary arteries. One report (Petch, 1973) included six deaths among 248 patients in whom the femoral (Judkins) technique was used, compared to no deaths among 111 patients catheterized by the brachial (Sones) technique. Four of the six died of sudden cardiovascular collapse while a preformed Judkins left coronary catheter was in the arch of the aorta. These four deaths were attributed to reflex bradycardia and hypotension in patients whose underlying cardiac disease made them unable to stand such an insult. Dr. Judkins reported fewer serious complications: of 445 consecutive studies, he reports two complications that eventually proved fatal. One was related to thrombosis of an abdominal aortic and iliac aneurysm, the other to congestive heart failure two days after an episode of arrhythmia during catheterization (Green, 1972). A third study (Chahine, 1972) of 478 Judkins and 413 Sones catheterizations found that while local arterial complications were significantly more common with the Sones technique, deaths were significantly more common with the Judkins technique. Adams (1973), in a national study conducted by polling catheterization laboratories, found an over-

all mortality of 0.13% for brachial techniques, and 0.78% for femoral. Mortality in institutions performing less than 200 procedures per year was much higher than in institutions performing 800 or more. The increase in risk in small institutions was particularly pronounced if the femoral technique was used. It is possible that the Judkins technique, being easier than the Sones, is more likely to be used by persons with little experience in handling catheterization complications. Adams also found that the Sones technique led to more local arterial complications. While no consensus has been reached, many laboratories have used the Sones technique as standard, resorting to the Judkins when difficulty is encountered and in emergencies when time is important.

Attention has recently been directed to patient factors involved in the serious complications of catheterization. Chahine (1972) points out that the deaths in his study occurred in "...very ill patients with extensive three-vessel coronary disease who were being considered for saphenous vein bypass graft surgery." Two studies have implicated left main coronary artery disease as predisposing to catheterization-related death (Cohen, 1972; Lavine, 1972). Taken together, the two studies describe 62 patients with left main coronary artery disease, eight of whom either died at catheter-

ization or subsequently of a myocardial infarction sustained at catheterization. Three of these eight patients had been catheterized by the Judkins technique. All three had a cardiac arrest immediately after the introduction of a Judkins catheter into the left coronary ostium. These three deaths occurred in only eight patients studied by the Judkins technique. Five deaths occurred in the 54 patients on whom the Sones technique was used. Two had sudden bradycardia and intractible hypotension, two sustained myocardial infarcts that proved fatal, and one died suddenly five hours after the procedure. (The similarity between the three Judkins technique deaths and the four sudden deaths described by Petch (1973) is striking: all seven occurred with a left Judkins catheter in the aortic arch. However, Petch specifies that the left coronary artery had not been entered in his cases. Further, one of Petch's patients had mitral valve disease, apparently without coronary artery disease. The other three may or may not have had coronary artery disease.)

Both studies commenting on left main disease reported a high incidence of marked ischemic S-T depression (greater than two millivolts) and severe angina pectoris among such patients. Both suggest that in a patient suspected of having left main disease, catheterization should be performed with great caution until

the left main coronary artery is visualized and seen to be normal.

Patient risk factors were emphasized even more strongly in a report by Hildner (1973) of a prospective study of patients admitted to a hospital for catheterization. This report, entitled "Pseudo Complications of Cardiac Catheterization," describes the untoward events occurring within 48 hours before or 24 hours after scheduled but unperformed catheterizations. Among 1,036 procedures actually performed there were 26 catheterization-related complications, including six deaths. During the same period (among an unspecified number of catheterizations scheduled but not performed) there were 24 "pseudo complications," including 12 sudden deaths. The specific complications in catheterized and uncatheterized patients were strikingly similar; there was even one case of pericardial tamponade in each group. The authors point out that pericardial tamponade, an unusual event in the course of heart disease, would surely have been attributed to the catheterization procedure if it had taken place. They also point out that their apparent complication rate would have almost doubled and their mortality rate tripled if their scheduling had been slightly different.

It must be realized, of course, that the inclusion of patients whose catheterization had been cancelled

means that some seriously ill patients were selected into the "pseudo complication" group. Nevertheless, it is clear that candidates for catheterization may be severely ill, and are therefore at risk for death or infarction independent of the procedure.

Thus, one is led to consider the possibility that major complications of cardiac catheterization may be a manifestation of the patient's underlying disease in resopnse to the stress of the procedure. If so, the factors that predispose to catheterization complications should be similar to the factors that predispose to death and myocardial infarction related to the natural history of the disease.

Recent years have seen the emergence of data relating the findings of coronary arteriography to subsequent long-term prognosis. Friesinger (1970) studied 224 patients catheterized and evaluated on a 15 point scale. Each major artery was scored as zero for normal, one for trivial irregularities, two for a 50% to 90% stenosis, three for multiple 50% to 90% stenoses, four for one or more stenoses greater than 90%, and five for total obstruction. Five year survival for various groups was projected by life-table analysis. Patients with a total score less than three and no single vessel with a score of two or more were found to have the same projected five year survival (97%) as an unselected population of the same age. Patients with scores from four to nine had a 95% five year survival, while those

with scores of 10 or greater had a 47% five year survival, a statistically significant difference. The arteriogram appeared to be a more accurate prognostic tool than any clinical parameter.

Oberman (1972) reports 246 patients, 140 of whom had significant coronary artery disease, defined as a 50% or greater stenosis of one or more vessels. Projected two year survival for patients with no significant disease or one-vessel disease was approximately 95%; for patients with two- or three-vessel disease it was approximately 70%. Using discriminant function analysis, it was found that heart size, left anterior descending coronary artery stenosis, and left main coronary artery stenoses were the most reliable predictors of poor survival.

Bruschke (1973a) reported 590 patients studied at Cleveland Clinic in 1963 to 1965. All had 50% or greater stenosis of one or more vessels. Follow-up was five to nine years. Five year mortality was 14.6% in patients with one-vessel disease, 37.8% in patients with two-vessel disease, 53.8% in patients with three-vessel disease, and 56.8% in patients with left main coronary artery disease. In patients with single-vessel disease, lesions of the left anterior descending coronary artery tended to have a worse prognosis, although the differences were not statistically significant.

When the coronary arteriographic findings were combined with the ventriculography results (Bruschke, 1973b), the predictive accuracy was increased.

Webster (1974), also from Cleveland Clinic, reported on patients with severe (80% or greater) proximal stenoses. (These patients, catheterized between 1960 and 1965, were selected as examples of patients who would now be considered likely candidates for bypass surgery.) Four hundred sixty-nine patients with significant disease were followed a minimum of six years. Six year mortality was 20% for patients with single-vessel disease, 40% for patients with two-vessel disease, and 63% for patients with three-vessel disease. Patients were also classified by functional disability according to New York Heart Association criteria. Functional class correlated with the number of vessels seriously diseased: over 80% of patients who were class I (asymptomatic) had single-vessel disease, while over 80% of patients who were class IV (symptomatic at rest) had double or triple vessel disease. But anginal severity had prognostic significance within the groups having one-, two-, or three-vessel disease. Patients within each anatomic group had a more grave prognosis if their angina symptoms were more severe.

Twenty-nine patients with severe left main coronary artery lesions were found, eight without and 21

with severe right coronary artery lesions. Mortality was 50% (four of eight) in the former subgroup, and 71% (15 of 21) in the latter. Both mortality rates are slightly higher than the rates for roughly equivalent lesions: combined left anterior descending and circumflex arteries (47%), and three-vessel disease (63%). The group with left main coronary artery stenosis also experienced high catheterization-related mortality: one patient died one day and another three days after catheterization.

Because patient populations and methods of evaluating the severity of coronary artery disease varied from study to study, numerical comparison of these studies is not valid. But by all methods used, severe coronary artery disease as determined by catheterization carried a poor prognosis.

While many studies have explored the relationship of clinical and angiographic findings to long-term survival, only left main coronary artery disease has been reported as a factor in catheterization-related death. While these studies implicate left main lesions, they do not compare the rates of catheterization-related mortality in patients with and without that lesion. Nor have they examined predictors for morbidity and mortality.

The present study is a review of 800 consecutive

coronary angiography studies performed at the Yale-New Haven Hospital. Three questions were addressed:

1) What factors can be used to predict a high risk of catheterization-related death?

2) What factors, _including_ catheterization data, characterize those patients dying in relation to catheterization?

3) Are the factors associated with catheterization-related death the same as those related to poor long-term prognosis?

Materials and Methods

From September 1, 1970, through September 25, 1973, 800 adult patients had cardiac catheterization with coronary angiography at Yale-New Haven Hospital. As will be detailed below, all patients with catheterization-related mortality and all but one with catheterization-related myocardial infarction had atherosclerotic coronary artery disease without any other complicating lesions, i. e., valvular, congenital, or myocardial disease. For analysis, a group of 223 patients with "pure" coronary artery disease was identified from the overall group of 800. This group excluded patients with any cardiomyopathy, congenital heart disease, or valvular disease. An exception to the last exclusion was mitral regurgitation thought to be due to ischemic damage to papillary muscles.

1) Mortality and Morbidity Related to Catheterization

The records of all 800 patients were searched for cases of catheterization-related death and myocardial infarction. "Catheterization-related" death was defined as a mortality which occurred during the procedure, or related to a significant complication taking place within five days of the procedure. Two patients who were clearly *in extremis*, with shock, anuria, coma, and congestive heart failure before the procedure, died soon afterward,

but were excluded from consideration. "Catheterization-related" myocardial infarction included any patient who was noted to have symptoms and electrocardiographic or enzymatic signs of myocardial infarction within five days of the procedure.

Clinical information was gathered on each patient's age, sex, severity of angina pectoris, and exercise test results. Angina pectoris was graded on a scale modified from the New York State Heart Association criteria for congestive heart failure symptoms: class I patients are asymptomatic, class II patients have symptoms on heavy exertion, class III on minimal exertion, and class IV patients have symptoms at rest. Exercise test results were grouped as negative, positive (ischemic electrocardiographic changes with exercise), or markedly positive (greater than two millivolt S-T depression).

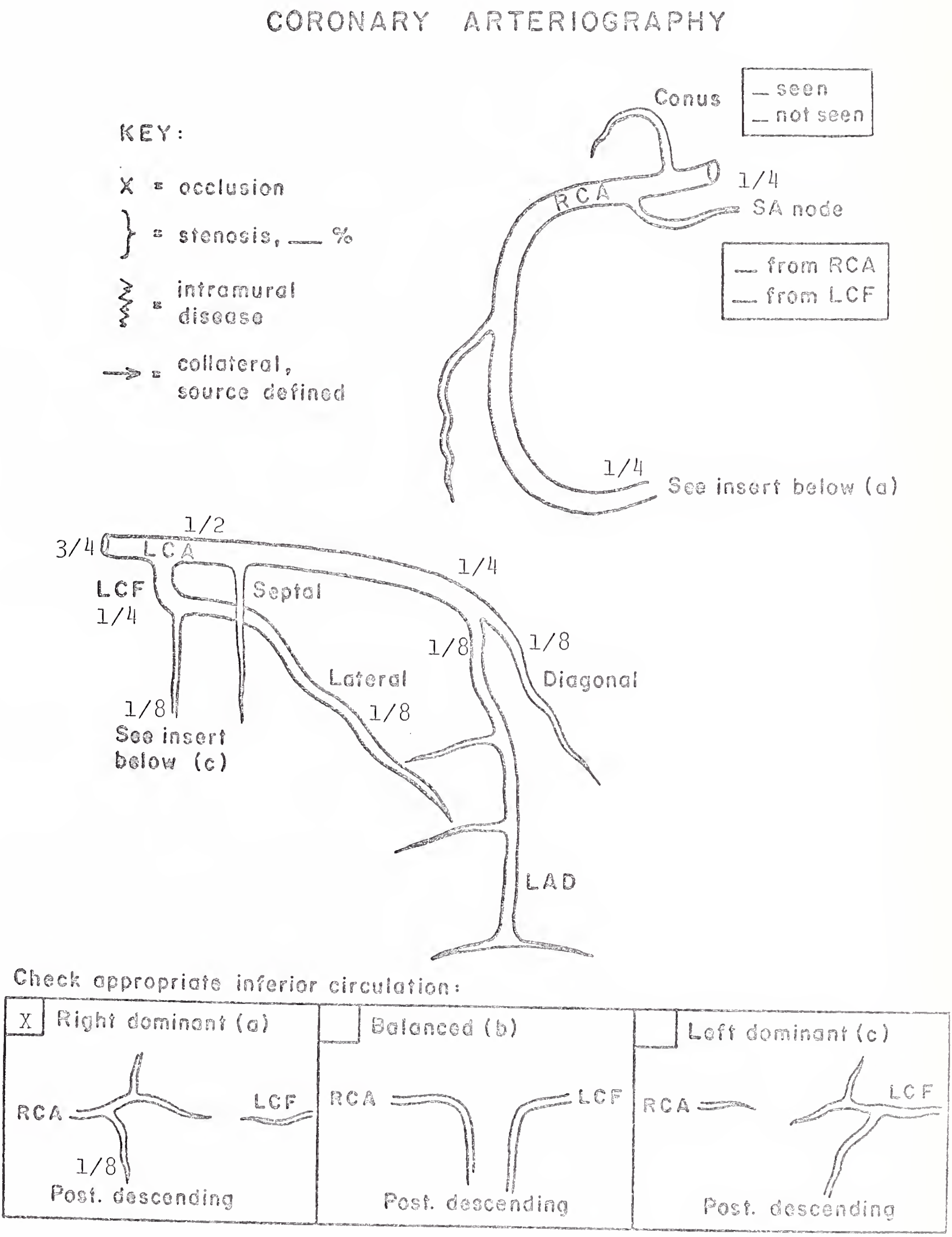
Information was analyzed with regard to each patient's catheterization: The technique by which each patient was catheterized--Sones, Judkins, or both--was noted. Coronary dominance was described as right, left, or balanced, using the system of Schlessinger (1940) with the primary criterion being the artery supplying the posterior descending artery.

Mitral regurgitation and left ventricular contraction pattern were evaluated in all patients by power

injection of contrast material into the left ventricle. Mitral regurgitation was evaluated on a scale of zero to four plus by the Amplatz criteria (Sellers, 1964). Left ventricular wall contraction abnormalities were grossly segregated as involving up to 25% of the ventricle, 25% to 50%, or greater than 50%. The location of the abnormality was grouped as anterolateral, apical, inferior, combinations of these locations, or "diffuse."

For analysis of the coronary anatomy, a hemodynamically significant lesion was defined as a stenosis of at least 50% of the internal lumen. An "impairment of circulation" value was computed on a scale of zero to eight according to the following formula (illustrated in Figures 1 and 2): If a patient was of right, balanced, or indeterminate dominance (Figure 1), three fourths of the circulation to his left ventricle was assumed to pass through the left main coronary artery to the bifurcation into left anterior descending (LAD) and left circumflex (LCF), half through the proximal LAD to small septal arteries and the distal LAD, one quarter through the distal LAD to the diagonal branch and small branch arteries, and one eighth through the LAD's first diagonal branch; one quarter through the main circumflex to its branches, one eighth through the circumflex marginal, and one eighth through the circumflex atrioventricular groove; one quarter through the

FIGURE 1

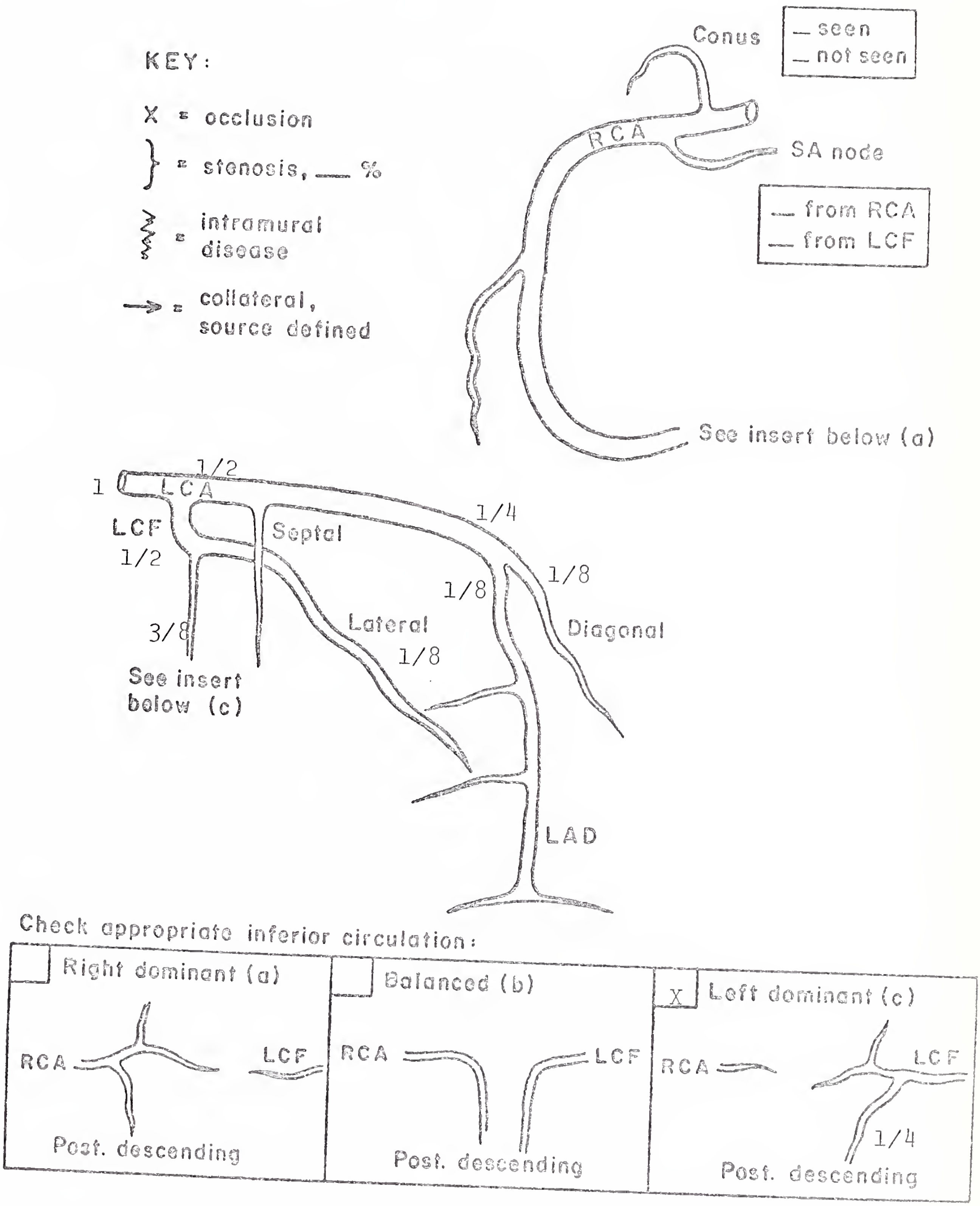

CORONARY ARTERIOGRAPHY
KEY:
X = occlusion
} = stenosis, ___ %
= intramural disease
= collateral, source defined
Conus
__ seen
__ not seen
RCA
1/4
SA node
__ from RCA
__ from LCF
1/4
See insert below (a)
1/2
3/4
LCA
LCF
1/4
Septal
1/4
1/8
1/8
Lateral
1/8
Diagonal
1/8
See insert below (c)
LAD
Check appropriate inferior circulation:
X
Right dominant (a)
RCA
LCF
1/8
Post. descending
Balanced (b)
RCA
LCF
Post. descending
Left dominant (c)
RCA
LCF
Post. descending

proximal right coronary artery (RCA), distal RCA, and the posterior descending. In this scoring system, for example, if a patient had a significant lesion of the left main, he had a score of six for his left-sided circulation regardless of any other disease on the left side. A lesion in the proximal RCA, distal RCA, or posterior descending artery would add two to the score. In a patient with a left dominant system (Figure 2), all of the circulation was assumed to pass through the left main, one half through the circumflex, three eighths through the circumflex atrioventricular groove, and one fourth through the posterior descending; values for the LAD were unchanged, and the RCA was considered of no consequence, supplying only the right ventricle.

As will be detailed below, all patients who suffered catheterization-related mortality were noted to have significant lesions either of the left main coronary artery or of its two main branches, the proximal LAD and the main LCF. For comparison, all patients with left main lesions were identified as a group, as were those with the comparable combined LAD and LCF lesions. In addition to the information mentioned above, these patients were studied with regard to hypertension, diabetes, hyperlipidemia, left ventricular end-diastolic pressure, and cardiac index. Comparisons were made by the chi-square test with Yates's correction for qual-

FIGURE 2

CORONARY ARTERIOGRAPHY



itative variables. For quantitative variables, the means and their standard errors were compared using Student's t-test.

2) <u>Prognostic Implications of Cardiac Catheterization Data</u>

To study the prognostic value of catheterization data compared to the prognostic value of other measures of coronary artery disease, questionaires have been sent to all patients with "pure" coronary artery disease. Only preliminary data are available at this time.

<u>Method of Coding for Computer Analysis</u>

Information from each patient's catheterization report was recorded on the coding form seen in Figure 3. Spaces 7 and 8 refer to the quality of the right and left coronary angiograms. Space 9 refers to coronary dominance, as described above. The patient's age at the time of catheterization was entered in spaces 16-17. Death was coded in months from catheterization; if the patient was alive, it was coded <u>99</u>. The patient's sex was coded in space 20. "Bypass graft" refers to saphenous vein bypass grafting. The entry was coded as the time between catheterization and surgery, or as <u>99</u> if surgery was performed before catheterization, or as <u>00</u> if it was not performed. The patient's class of angina pectoris was coded in space 24 on a scale of 1 to 4 for classes I to IV. In space 25, results of

FIGURE 3

Name ______________________ Date of Entry ______________

1 2 3 4 5 6
Unit No.

7 R, 8 L
Quality of study
1=adequate
2=inadequate

9
Dominance
1= right
2= left
3= balanced
4= indeterminate

10 11
Duration observed to present (months)

16 17
Age

Cath. Date ______________

18 19
Death (mths.)
9 9 if alive

20
Sex

22 23
Bypass Graft

Enter 0 0 if not applicable,
duration if done during study,
99 if done at entrance to study.

28
Mit. Regurg.
0= none
1= 1+
2= 2+
3= 3+
4= 4+

29
Dyskinesis
0= none
1= 25%
2= up to 50%
3= more than 50%.

30
Dyskinesis location
1= anterolateral
2= apex
4= inferior
8= diffuse

Vessel	Parent Vessel	Runoff
A) RCA-prox. to marg.	31	32
B) RCA-dist. to marg.	35	36
C) RCA-post descending	39	40
D) RCA-RV marginal	43	44
E) LCA-main	47	48
F) LAD-prox. to 1st septal	51	52
G) LAD-dist. to 1st septal	55	56
H) LAD-1st diagonal	59	60
I) LCF-main	63	64
J) LCF-marginal	67	68
K) LCF-A-V groove	71	72
L) Pulmonary conus	75	76

24
Angina
1= class I
2= class II
3= class III
4= class IV

25
Exercise test
1= negative
2= positive
3= ~~+++~~
4= too sick
5= not done or equivocal

26
Technique
1= Sones
2= Judkins
3= both

27
Complications
D= death
M= M.I.
E= *in extremis*
blank= none

KEY
1= not seen
2= normal
3= single stenosis (more than 50%)
4= multiple stenoses
5= diffusely narrowed
6= occluded
7= non-occlusive disease

79
Circulation Impairment Score

80
Coronary artery disease
0=absent
1=present

____
Signed

the patient's exercise test were coded: 1 for negative, 2 for positive, 3 for markedly positive (greater than two millivolts S-T depression), 4 if the test was omitted because the patient was too ill to be exercised, and 5 if the test was equivocal or was not done for other reasons. In space 26 the catheterization technique was coded: 1 for Sones, 2 for Judkins, 3 for both. In space 27, death or myocardial infarction related to catheterization or the fact that the patient was *in extremis* when catheterized were coded. Mitral regurgitation was coded on a scale of 0 to 4, and dyskinesis of contraction on a scale of 0 to 3, as described above. Dyskinesis location was coded by the scale shown, and by the *sum* of the specified locations if it was present in more than one.

Arteries were entered by the code under "KEY" in the figure, with one value for the artery and one for its runoff. On the coding form, an occlusion or 99% stenosis was coded as a 6, a stenosis of 50-98% as a 3, intramural disease (and one aneurysm) as a 7, and other cases according to the key on the coding form. Stenoses are usually read as 50%, 75%, 90%, 95%, or 99%. These percentages generally overstate the accuracy of the readings. It has been found that any stenosis that can be distinguished as such from "intramural disease" is at least 50%. The apparent severity of a stenosis

depends on the angle from which it is viewed. In fact, some stenoses detected at autopsy are missed at angiography. Readings of "high-grade stenosis" or "no stenosis" are more reliable (Kemp, 1967; Vlodaver, 1973). In space 79, the impairment of circulation score described above was entered on a scale of 0 to 8. In space 80, all patients with coronary artery disease were coded 1.

Analyses were carried out at the Yale Computer Center using the "CROSSTAB" (cross-tabulation) command of Data-Text computer language (Armor, 1972). Frequently, data were regrouped and reanalyzed on a calculator, using the chi-square test with Yates's correction.

These factors were analyzed for correlation with survival as of the last recorded follow-up. Since follow-up is incomplete at this time, all results must be considered as preliminary. When complete data are available, the life-table method of predicting survival (Cutler, 1958) will be used to evaluate prognostic significance of the factors coded. This method predicts survival for a group of patients followed for varying lengths of time. The study is divided into periods of time after catheterization, and patients who survive through or die during each period are used to determine the risk during that period. Patients whose follow-up ends during a period are treated as "withdrawls" and

are not used to determine the risk for that or subsequent periods. Patients on whom bypass graft surgery is performed will be treated as "withdrawls" from the study at the time of their surgery. This will bias the study somewhat, as patients are obviously selected for surgery. Patients who died related to the catheterization itself are not included in the analysis of long-term prognosis.

Results

1) Mortality and Morbidity Related to Catheterization

Of the 800 cardiac catheterizations, there were seven procedure-related deaths. All seven had isolated coronary artery disease as their only etiology. As shown in Table I, four had left main coronary lesions. The other three had lesions of the proximal left anterior descending and of the left circumflex (LAD+LCF), a combination that is hemodynamically equivalent to a left main lesion. All also had other lesions, including impairment of the right-sided circulation in six (counting A.M., who had a left-dominant system with left main and circumflex lesions).

Six of the seven had angina at rest (class IV), compared to 54 of 203 patients who had no complications ($P<0.005$). The seventh had a markedly positive exercise test (angina and four millivolt S-T depression) at zero watts on a bicycle ergometer--class III.

All seven of the patients who died related to catheterization had circulation impairment scores of six or greater, while only 92 of 203 patients who suffered no catheterization-related complications had scores of six or more ($P<0.025$). The mean circulation impairment score for the patients who died was 7.71 ± 0.76; for the patients who had no complications it was 5.51 ± 1.88, significantly lower ($P<0.0001$).

Four of the seven had left main coronary artery lesions, while only 16 of 203 patients with no complications had such lesions ($P<0.005$). Three of seven had LAD+LCF lesions, a higher but not significantly different proportion than the 30 of 203 who had no complications ($P>0.10$). Four of seven who died were female, compared with only 34 of 203 uncomplicated cases ($P<0.05$). Six of the seven had significant disease of all three arterial systems, compared to 55 of 203 who had no complications ($P<0.005$).

No correlation was found between catheterization-related death and age, coronary dominance, mitral regurgitation, dyskinesis extent, and dyskinesis location.

In six patients who died related to catheterization, only the Sones technique was used; in the seventh, both the Sones and Judkins methods were needed. Of the group of 224, the Sones technique was used in 202 patients, the Judkins technique alone in 11, and both in 11 patients.

On the premise that arterial disease of the left main coronary artery or of the proximal LAD and LCF represented a high risk, those patients who died were compared to the patients with either of these lesions who survived catheterization. The patients who died were significantly more likely to be diabetic--four of seven who died, seven of 53 who survived ($P<0.05$),

and to have a low cardiac index--1.46±0.14 for those who died, 2.44±1.03 for those who survived ($P<0.01$).

The total left main and LAD+LCF groups (including the patients who died) were compared to each other. There were 24 patients with left main lesions and 36 with LAD+LCF among the 223 patients with pure coronary artery disease. There were no significant differences between the two groups with regard to age, sex, presence of hypertesion, diabetes, or hyperlipidemia, previous myocardial infarction, exercise test results, left ventricular end diastolic pressure, cardiac index, dyskinesis of contraction, mitral regurgitation, or presence of right coronary artery lesions. Thus, the two groups could not be distinguished clinically or by catheterization determination of left ventricular function.

Catheterization-related mortality did occur with greater rapidity in the left main patients than in the LAD+LCF patients (Table 1). Three left main patients died on the catheterization table, going rapidly into shock before any arrhythmia developed. The fourth had arrhythmias during the procedure which were successfully treated at the time, but which recurred four hours later and did not respond to treatment.

Based on the experience of three previous deaths in patients with left main disease, nonselective opacification of the left main coronary was attempted in

TABLE 1 DEATHS

Patient	Sex	Coronary Lesions		Clinical Data	Timing	Mode of Exodus
M.P.	M	Left Main	LAD LCF RCA	Class 1V LV gram>50%	4 hrs. post cath.	PAT, V tach. during cath.; V tach. after cath., unresponsive to Rx.
S.S.	M	Left Main	LAD LCF RCA	Class 111 Ex. test +++ at zero watts. LV gram-25%	During	Vomited after LV gram, shock, V tach., q waves.
D.S.	F	Left Main	LAD	Class 1V LV gram-50%	During	Shock after RCA arteriogram.
A.M.	M	Left Main	LAD LCF-Left Dominant	Class 1V 4mm. ST with angina LV gram-25%	During	Shock 2 minutes after single LCA arteriogram.
L.M.	F	LAD+LCF	LAD (distal) RCA	Class 1V LV gram-25%	34 hrs.	(Judkins and Sones). Hypotensive, low output, bowel infarct, 2 hours post cath.
J.P.	F	LAD+LCF	RCA	Class 1V LV gram->50%	80 hrs.	RBBB post cath. Died suddenly.
M.B.	F	LAD+LCF	LAD (distal) LCF	Class 1V MI 12 days previous. LV gram->50%	48 hrs.	Hypotension 1 day post cath.

the last patient, A.M. He was suspected of having a left main lesion because he had angina at rest, marked (four millivolt) S-T depression in most of the precordial leads during attacks of angina, and because he became dyspneic during his angina attacks. At catheterization, several sinus of Valsalva injections were performed in an attempt to opacify the left system. Some of it was indeed visualized, but the sinus overlay the left main coronary artery. In addition, the distal vessel filled poorly. Finally, one selective opacification was performed, confirming a high grade proximal stenosis. Approximately two minutes after this single selective injection of the left system, the patient went into shock unresponsive to all forms of therapy, and died within an hour.

Of the LAD+LCF patients, L.M. became hypotensive with a low cardiac output two hours after the procedure. She expired 34 hours after the procedure, probably of multiple systemic infarctions secondary to the low output state. J.P. developed right bundle branch block soon after the procedure, which was presumed to be due to a myocardial infarction. She seemed to be recovering until her sudden death about 80 hours after the procedure. M.B. became hypotensive one day after the procedure and died the next day. At autopsy she was found to have an evolving myocardial infarct (see below).

Although similar to each other, the left main and LAD+LCF groups did differ from the pure coronary artery disease group as a whole. Twenty-one of the 24 left main patients had class III or IV angina, as did 24 of 36 LAD+LCF patients, but only 70 of 164 with neither lesion. Either group taken alone was significantly different from the group with neither lesion ($P<0.0001$ for the left main group, $P<0.025$ for the LAD+LCF group); taken together, $P<0.0001$.

Autopsies are available on four of the seven patients (Table 2). In no patient could evidence of dissection or embolization of a coronary artery be found. In M.B. there was evidence of an infarct about one week old that was suspected but could not be confirmed clinically. In A.M. there was a 75% stenosis of the right coronary artery that had been interpreted as "intramural disease" by angiography.

Figure 4 is a summary of the significant differences among the group of patients with pure coronary artery disease, the group with left main or LAD+LCF lesions, and the group who died related to catheterization. Note that it is not a flow diagram. The arrows are labeled with the parameters that are found significantly more commonly in the group to which the arrow points than in the group from which the arrow points.

TABLE 2 AUTOPSY FINDINGS

Name	Sex	Lesion	Time and Mode of Exodus	Autopsy Findings
D.S.	F	Left Main	During cath.	Large, calcified atheromatous plaque at the origin of the left main coronary artery. Possible fresh infarct in the superior, posterior LV. Diffuse myocardial scanning.
A.M.	M	Left Main	During cath.	50% Left Main. 75% RCA. 90% LCF. 80-85% LAD and diagonal.
M.B.	F	LAD-LCF	48 hours post cath.	Extenxive old and lateral infarct with LV aneurysm including papillary muscles. Recent (7 days old) septal infarct. Pulmonary infarct. Diffuse coronary atheromata.
L.M.	F	LAD-LCF	34 hours post cath.	Recent(<1 day) massive septal infarct. Old diffuse scarring. Occlusions of LAD, LCF, RCA. 80% narrowing of left main. Ischemic colitis, infarcts of liver and spleen.

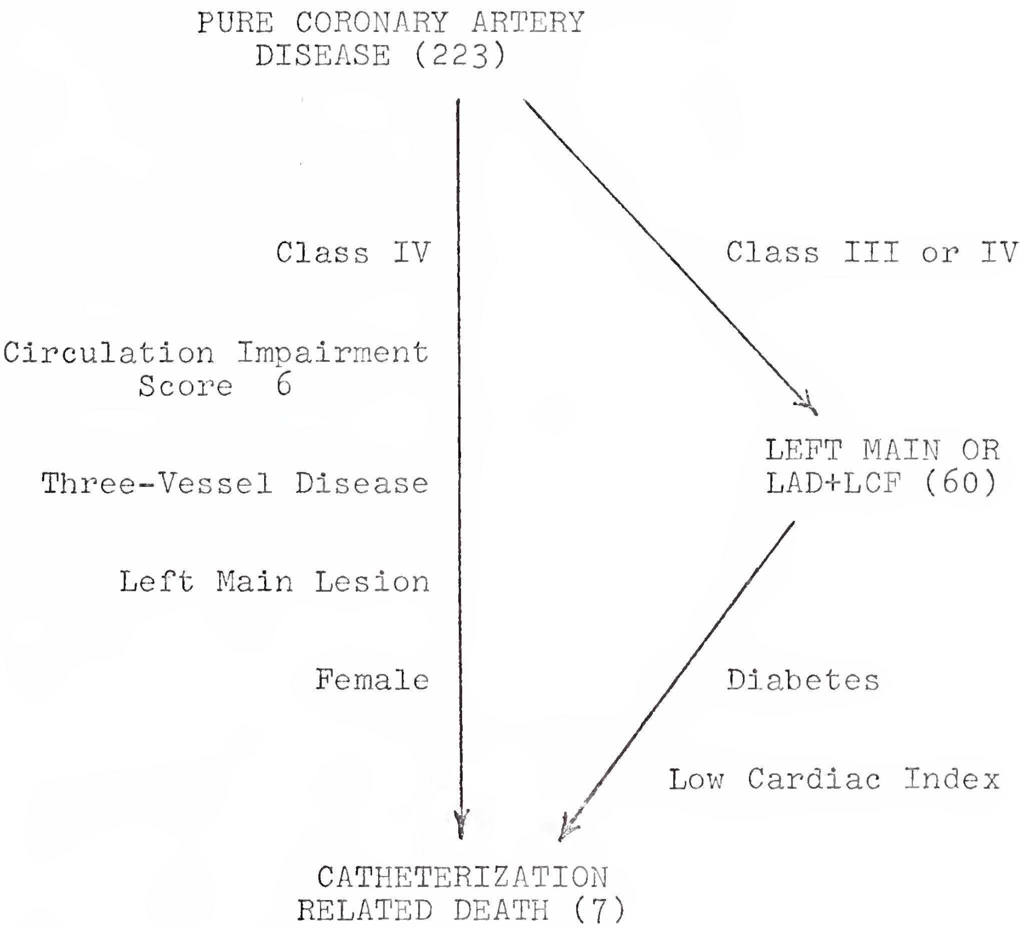

PURE CORONARY ARTERY DISEASE (223)
Class IV
Circulation Impairment Score 6
Three-Vessel Disease
Left Main Lesion
Female
Class III or IV
LEFT MAIN OR LAD+LCF (60)
Diabetes
Low Cardiac Index
CATHETERIZATION RELATED DEATH (7)

FIGURE 4

The patients who suffered myocardial infarcts related to catheterization are summarized in Table 3. The first six patients seem to resemble those patients who died related to the procedure. They all have three-vessel coronary disease, left main or LAD+LCF lesions, and four of six have class IV angina or markedly positive exercise tests. The second set of six seem to be a less seriously ill group, with most having negative exercise tests and no more than two vessels diseased in five cases. Chest pain caused termination of the catheterization before angiography was performed in the sixth.

In one case, R.L., the infarction seems to have been caused by dissection of the proximal right coronary artery. During the left ventriculogram, the catheter recoiled out of the ventricle. The RCA was visualized at that time, but the catheter apparently traumatized the right coronary ostium. When a later attempt was made to catheterize the right coronary, it was totally occluded in its proximal portion. At about the same time, electrocardiographic changes of a posterior infarction were noted. In another case, S.B., review of the films showed that the catheter had been advanced through a proximal right coronary stenosis.

Although some criteria distinguished those patients who died related to catheterization from those who had

TABLE 3 PART 1 MYOCARDIAL INFARCTIONS

Patient	Sex	Coronary Lesions		Clinical Data	Timing	ECG	Comments
V.D.	F	LAD+LCF	RCA	Class 11 (angina).	During	Inferior	V tach. twice during procedure, once after LCA injection.
K. J.	M	LAD+LCF	RCA	Class 111. LV gram>50%	12 hrs. after	Anterior	
E.M.	M	LAD+LCF	RCA	Class 1V. LV gram 25%.	During	Inferior	
C.H.	M	Left Main	RCA LAD LCF	Exercise test positive-0.5mm.	End of cath.	No change	Enzyme elevation, hypotension. Judkins and Sones techniques.
K.P.	M	Left Main	RCA LAD	Class 1V. LV gram 50%	During	Inferior	
R.L.	M	Left Main	RCA LAD LCF	Class111. Exercise test positive 3 mm.	During	Inferior	Dissection of proximal RCA.

TABLE 3 PART 2 MYOCARDIAL INFARCTIONS

Patient	Sex	Coronary Lesions	Clinical Data	Timing	ECG	Comments
S.B.	M	RCA	Class lV	During	Inferior	Catheter advanced through RCA stenosis. AF during study.
A.P.	M	RCA LCF	Exercise test negative.	5 days after	No change	Enzyme elevations at 5 days, no ECG changes.
W.D.	M	RCA LAD	Exercise test positive. LV gram 25%.	7 hours after	Antero-lateral	Bradycardia and hypotension 7 hours after cath. ECG changes of subendocardial MI with slight enzyme elevation.
P.P.	M	LAD	Exercise test negative. LV gram 25%.	During	Lateral	
R.M.	M	None	Dyspnea, no angina. LV gram 50%.	3 hours after	Inferior and Anterior	Judkins and Sones techniques, polyurethane catheters, cardiomyopathy.
B.T.	F	?	Exercise test negative. LV gram>50%.	During LV gram	Inferior	Judkins technique, polyurethane catheters, femoral occlusion, requiring bypass.

no complications, none distinguishes the patients who had myocardial infarcts related to catheterization. No statistically significant differences between the infarct and uncomplicated groups were found. Class of angina, circulation impairment scores, sex, presence or absence of three-vessel disease, left main coronary artery lesions, LAD+LCF lesions, and cardiac index were compared.

2) <u>Prognostic Implications of Cardiac Catheterization Data</u>

Preliminary analysis of the available follow-up data suggests that long term survival may correlate only with class of angina and circulation impairment score. The average length of follow-up was 8-1/4 months. Those patients who died after catheterization documentation of their coronary lesions had a greater incidence of circulation impairment scores of six or greater (21 of 26) as compared to those still living (98 of 190), $P<0.01$. Class III or IV angina was also more frequent in those who died (25 of 26) than in the survivors (107 of 191), $P<0.0005$.

There were no significant associations between long term death and the number of systems diseased, sex, left main or LAD+LCF lesions, exercise test results, mitral regurgitation, or dyskinesis.

Discussion

1) Predictors of Mortality Related to Catheterization

Of all clinical parameters evaluated, the patient's functional class of angina pectoris was found to be the best predictor of a high risk at catheterization. All the patients who died had class IV angina or class III with a markedly positive exercise test. The mortality among such patients was 9.9%.

2) Catheterization Data Relating to Mortality

A high risk of catheterization-related mortality was associated with extensive coronary artery disease. Not only were left main coronary artery patients implicated, but also those with an equivalent physiologic deficit--both LAD and LCF stenoses. There was no significant difference in catheterization-related mortality between the left main and LAD+LCF groups, suggesting that the danger inherent in a left main lesion arises primarily from its hemodynamic effects.

These results suggest that patient risk factors play a major role in determining the risk of catheterization-related mortality. If so, a major reduction in mortality may have to await major advances in the treatment of cardiogenic shock, in the same way that the major reduction in mortality due to ventricular fibrillation that occurred several years ago required the theraputic advances of closed chest cardiac massage

and quick external defibrillation. Unfortunately, no such advance in the treatment of cardiogenic shock seems forthcoming.

In contrast to risk of death, risk of myocardial infarction was not correlated with any of the factors studied. This suggests that patient risk factors are not the strongest determinants of catheterization-related myocardial infarction. Technical factors and chance errors seemed more important. It may be that a randomly occurring mild insult that produces a mild myocardial infarction in a relatively healthy patient can cause death in a patient with class IV angina.

3) Prognostic Implications of Cardiac Catheterization Data

Assuming that the preliminary analyses of factors relating to long-term prognosis are borne out, class of angina and circulation impairment score are the only factors correlated with late death after cardiac catheterization. These data are in reasonable agreement with the studies by Friesinger (1970), Oberman (1972), Bruschke (1973a, 1973b), and Webster (1974), allowing for the different systems of quantitating arteriographic findings. Class III or IV angina and a high circulation impairment score were found in those with long-term mortality. Class IV angina or a markedly positive exercise test, combined with left main or LAD+LCF lesions, also correlated with catheterization-related mortality

in our study.

The similartiy of acute and long-term correlates of mortality suggests that the degree to which the host is diseased may be the primary factor contributing to both. The patients with the highest risk of catheterization-related mortality seem to be the most symptomatic patients, and these seem also to be the patients with the worst long-term prognosis from atherosclerotic heart disease. It is reasonable to suppose that the high catheterization risk represents the result of stress in a very precarious patient population.

Since it seems possible to predict with fair accuracy the patients who will be at high risk due to catheterization, what use can be made of this information? These patients are high priority candidates for saphenous vein bypass grafting as well as high risk catheterization candidates. Definition of the precise coronary anatomic deficit is essential, and the patients with the greatest risk need catheterization the most.

The use of external or intraaortic assist devices for support of these patients during catheterization is a question deserving of investigation.

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